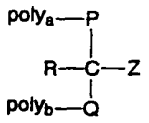
WHAT IS CLAIMED IS:

1. A polymeric derivative represented by the structure



wherein $poly_a$ and $poly_b$ are nonpeptidic and substantially nonreactive water soluble polymeric arms that may be the same or different, wherein C is carbon, wherein P and Q comprise linkage fragments that may be the same or different and join polymeric arms $poly_a$ and $poly_b$, respectively, to C by hydrolytically stable linkages in the absence of aromatic rings in said linkage fragments, wherein R is a moiety selected from the group consisting of H, substantially nonreactive moieties, and linkage fragments having attached thereto by a hydrolytically stable linkage in the absence of aromatic rings one or more nonpeptidic and substantially nonreactive water soluble polymeric arms, and wherein Z comprises a moiety selected from the group consisting of moieties having a single site reactive toward nucleophilic moieties, sites that can be converted to sites reactive toward nucleophilic moieties, and the reaction product of a nucleophilic moiety and moieties having a single site reactive toward nucleophilic moieties.

2. The polymeric derivative of Claim 1 wherein said hydrolytically stable linkages are selected from the group consisting of amide, amine, ether, carbamate, thiourea, urea, thiocarbamate, thiocarbonate, thioether, thioester, and dithiocarbamate linkages.

3. The polymeric derivative of Claim 1 wherein said nucleophilic moieties are selected from the group consisting of amino, thiol, and hydroxyl moieties.

4. The polymeric derivative of Claim 1 wherein said nucleophilic moiety is a biologically active molecule.

5. The polymeric derivative of Claim 4 wherein said biologically active molecule is selected from the group consisting of polypeptides, polynucleotides, and lipids.

6. The polymeric derivative of Claim 1 wherein said nucleophilic moiety is a solid surface or a particle.

7. The polymeric derivative of Claim 6 wherein said solid particle is a liposome.

8. The polymeric derivative of Claim 1 wherein Z is selected from the group consisting of carboxyl, hydroxyl, activated carboxyl, activated hydroxyl, and conjugates of activated carboxyl or hydroxyl sites and molecules having at least one reactive nucleophilic moiety.

9. The polymeric derivative of Claim 1 wherein Z comprises a moiety selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde, vinylsulfone, maleimide, iodoacetamide, and iminoesters.

10. The polymeric derivative of Claim 9 wherein said active ester is N-hydroxylsuccinimidyl ester and said active carbonates are selected from the group consisting of N-hydroxylsuccinimidyl carbonate, *p*-nitrophenylcarbonate, and trichlorophenylcarbonate.

11. The polymeric derivative of Claim 1 wherein said nonpeptidic polymeric arms are selected from the group consisting of poly(alkylene oxides), poly(oxyethylated polyols), and poly(oxyethylated glucose).

12. The polymeric derivative of Claim 1 wherein said nonpeptidic polymeric arms are selected from the group consisting of poly(ethylene glycol), poly(vinyl alcohol), poly(propylene glycol), poly(oxyethylated glycerol), poly(oxyethylated sorbitol), poly(oxyethylated glucose), poly(oxazoline), poly(acryloylmorpholine), and poly(vinylpyrrolidone).

13. The polymeric derivative of Claim 1 wherein said nonpeptidic polymeric arms are linear mPEGs of molecular weight of from about 50 to 50,000.

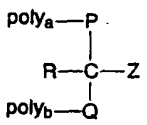
14. The polymeric derivative of Claim 1 wherein said linkage fragments P and Q comprise hydrolytically stable linkages in the absence of aromatic rings to one or more nonpeptidic and water soluble polymeric arms.

15. The polymeric derivative of Claim 1 wherein R comprises a linkage fragment attached by a hydrolytically stable linkage in the absence of aromatic rings to a nonpeptidic and substantially nonreactive water soluble polymeric arm.

16. The polymeric derivative of Claim 15 wherein R is represented by the general structure -M-$poly_d$, wherein $poly_d$ is said polymeric arm and M is said linkage fragment.

17. The polymeric derivative of Claim 1 wherein Z further comprises a linkage fragment attached by a hydrolytically stable linkage in the absence of aromatic rings to a nonpeptidic and substantially nonreactive water soluble polymeric arm.

18. A polymeric derivative represented by the structure



wherein $poly_a$ and $poly_b$ may be the same or different and are selected from the group consisting of linear poly(ethylene glycol), poly(vinyl alcohol), poly(propylene glycol), poly(oxyethylated glycerol), poly(oxyethylated sorbitol), poly(oxyethylated glucose), poly(oxazoline), poly(acryloylmorpholine), and poly(vinylpyrrolidone); wherein C is carbon; wherein P and Q comprise linkage fragments that may be the same or different and join polymeric arms $poly_a$ and $poly_b$, respectively, to C by hydrolytically stable linkages selected from the group consisting of amide, amine, ether, carbamate, thiourea, urea, thiocarbamate, thiocarbonate, thioether, thioester, and dithiocarbamate linkages; wherein R is a moiety selected from the group consisting of H, substantially nonreactive moieties, and linkage fragments having attached thereto by a hydrolytically stable linkage in the absence of aromatic rings one or more nonpeptidic

and substantially nonreactive water soluble polymeric arms; and wherein Z comprises a moiety selected from the group consisting of carboxyl, hydroxyl, trifluoroethylsulfonate, isocyanate, isothiocyanate, N-hydroxylsuccinimidyl ester, N-hydroxylsuccinimidyl carbonate, *p*-nitrophenylcarbonate, trichlorophenylcarbonate, aldehyde, vinylsulfone, maleimide, iodoacetamide, and iminoesters.

19. A multi-armed monofunctional polymeric derivative that is the reaction product of at least one monofunctional nonpeptidic polymer derivative and a linker moiety having two or more active sites that form linkages with said monofunctional nonpeptidic polymer derivatives in the absence of aromatic moieties, wherein said linkages between said linker moiety and said monofunctional nonpeptidic polymer derivatives are hydrolytically stable.

20. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said linker moiety is selected from the group consisting of monohydroxy alcohols and monocarboxylic acids.

21. The multi-armed monofunctional polymer derivative of Claim 19 wherein said active sites on said linker moiety are nucleophilic moieties.

22. The multi-armed monofunctional polymer derivative of Claim 21 wherein said nucleophilic moieties are selected from the group consisting of amino, thiol, and hydroxyl moieties.

23. The multi-armed monofunctional polymer derivative of Claim 19 wherein said active sites on said linker moiety are electrophilic moieties.

24. The multi-armed monofunctional polymer derivative of Claim 23 wherein said electrophilic moieties are selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde, vinylsulfone, maleimide, iodoacetamide, and iminoesters.

25. The multi-armed monofunctional polymeric derivative of Claim 24 wherein said active esters are N-hydroxylsuccinimidyl ester and said active carbonates are selected from the group consisting of N-hydroxylsuccinimidyl carbonates, *p*-nitrophenylcarbonates, and trichlorophenylcarbonates.

26. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said hydrolytically stable linkages in the absence of aromatic rings are selected from the group consisting of amide, amine, ether, carbamate, thiourea, urea, thiocarbamate, thiocarbonate, thioether, thioester, and dithiocarbamate linkages.

27. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said monofunctionality is selected from the group consisting of carboxyl, hydroxyl, activated carboxyl, activated hydroxyl, and conjugates of activated carboxyl or hydroxyl sites and molecules having at least one reactive nucleophilic moiety.

28. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said monofunctionality is selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde,

vinylsulfone, maleimide, iodoacetamide, and iminoesters.

29. The multi-armed monofunctional polymeric derivative of Claim 28 wherein said active ester is N-hydroxylsuccinimide and said active carbonates are selected from the group consisting of N-hydroxylsuccinimide carbonates, *p*-nitrophenylcarbonates, and trichlorophenylcarbonates.

30. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said nonpeptidic polymeric derivative is selected from the group consisting of poly(alkylene oxides), poly(oxyethylated polyols), and poly(oxyethylated glucose).

31. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said nonpeptidic polymer derivative is selected from the group consisting of activated poly(ethylene glycol), poly(vinyl alcohol), poly(propylene glycol), poly(oxyethylated glycerol), poly(oxyethylated sorbitol), poly(oxyethylated glucose), poly(oxazoline), poly(acryloylmorpholine), and poly(vinylpyrrolidone).

32. The multi-armed monofunctional polymeric derivative of Claim 19 wherein said nonpeptidic polymer derivative is a linear mPEG of molecular weight of from about 50 to 50,000 and the multi-armed monofunctional polymeric derivative has two arms of said linear mPEG.

33. A material comprising a solid surface or particle having attached thereto compounds of the structure claimed in Claim 19.

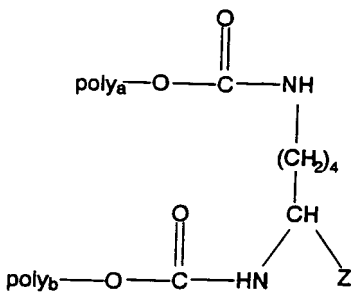
34. The material of Claim 33 wherein said solid surface or particle is a liposome.

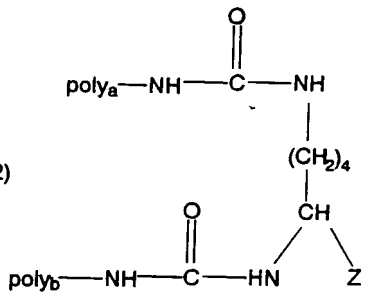
35. A biologically active structure comprising a biologically active molecule having attached thereto one or more compounds of the structure claimed in Claim 19.

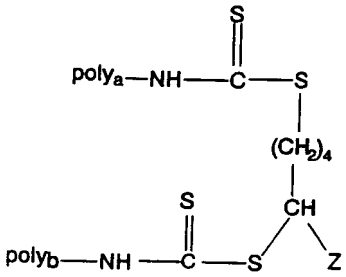
36. The biologically active structure of Claim 35 wherein said biologically active molecule is selected from the group consisting of polypeptides, polynucleotides, and lipids.

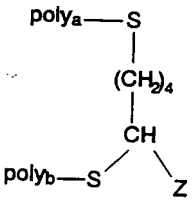
37. The biologically active structure of Claim 36 wherein said polypeptide is selected from the group consisting of asparaginase, catalase, ribonuclease, subtilisine, trypsin, and uricase.

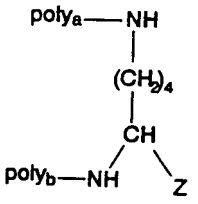
38. A two-armed polymeric derivative having a structure selected from the group consisting of:

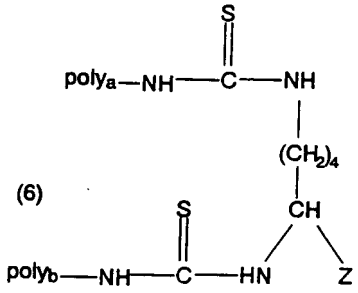
(1) 

(2) 

(3) 

(4) 

(5) 

(6) 

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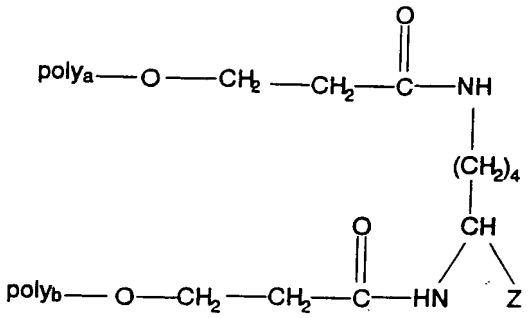

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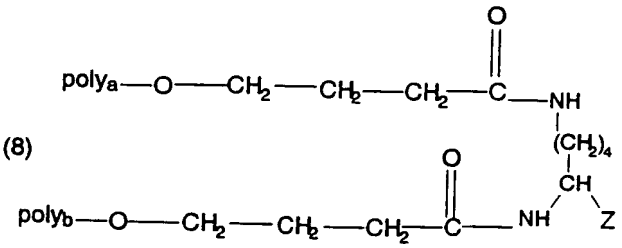

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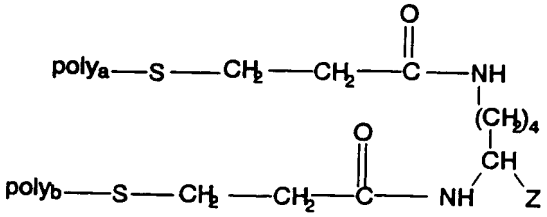

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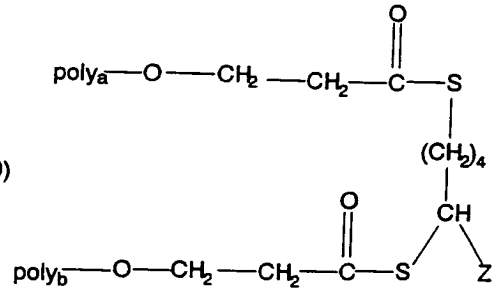

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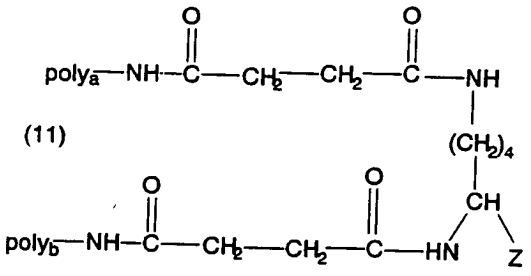

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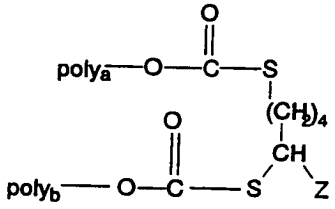

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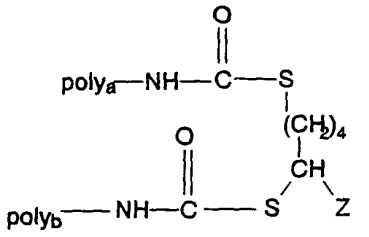
(13) 

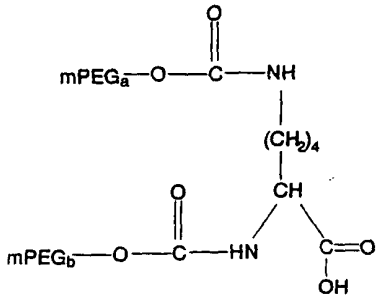
wherein $poly_a$ and $poly_b$ may be the same or different and comprise moieties selected from the group consisting of poly(ethylene glycol), poly(vinyl alcohol), poly(propylene glycol), poly(oxyethylated glycerol), poly(oxyethylated sorbitol), poly(oxyethylated glucose), poly(oxazoline), poly(acryloylmorpholine), and poly(vinylpyrrolidone) moieties; and wherein Z comprises a moiety selected from the group consisting of moieties having a single site reactive toward nucleophilic moieties, sites that can be converted to sites reactive toward nucleophilic moieties, and the reaction product of a nucleophilic moiety and moieties having a single site reactive toward nucleophilic moieties.

39. The two-armed polymeric derivative of Claim 38 wherein said reactive site is selected from the group consisting of carboxyl, activated carboxyl, hydroxyl, activated hydroxyl, and conjugates of activated carboxyl or hydroxyl sites and molecules having at least one reactive nucleophilic moiety.

40. The polymeric derivative of Claim 38 wherein Z comprises a moiety selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde, vinylsulfone, maleimide, iodoacetamide, and iminoesters.

41. The polymeric derivative of Claim 40 wherein said active ester is N-hydroxylsuccinimidyl ester and said active carbonates are selected from the group consisting of N-hydroxylsuccinimidyl carbonate, *p*-nitrophenylcarbonate, and trichlorophenylcarbonate.

42. A molecule having the structure



wherein $mPEG_a$ and $mPEG_b$ have the structure $CH_3-(CH_2CH_2O)_nCH_2CH_2-$, wherein n equals from 1 to about 1,150, and wherein n may be the same or different for $mPEG_a$ and $mPEG_b$.

43. The molecule of Claim 42 wherein n equals from 1 to about 570.

44. A method of synthesizing a multi-armed, water soluble, monofunctional polymeric molecule comprising reacting one or more nonpeptidic monofunctional polymers of the structure poly-W, wherein W is an active moiety providing the monofunctionality for the polymer, with a linker moiety having two or more active sites with which W is reactive, and forming hydrolytically stable linkages in the absence of aromatic rings between the monofunctional polymer and the linker moiety at the linker moiety active sites, the linker moiety having a reactive site for which said active moiety -W is not

reactive to provide the monofunctionality for the multi-armed molecule.

45. The method of Claim 44 wherein the method further comprises activating the reactive site after the multi-armed polymeric compound is formed with an electrophilic moiety.

46. The method of Claim 45 wherein the electrophilic moiety is reactive with nucleophilic moieties selected from the group consisting of amino, thiol, and hydroxyl moieties.

47. The method of Claim 44 wherein the active moiety W is an electrophilic moiety selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde, vinylsulfone, maleimide, iodoacetamide, and iminoesters.

48. The method of Claim 47 wherein the active ester is N-hydroxylsuccinimidyl ester and the active carbonates are selected from the group consisting of N-hydroxylsuccinimidyl carbonate, *p*-nitrophenylcarbonate, and trichlorophenylcarbonate.

49. The method of Claim 44 wherein the active moiety W is a nucleophilic moiety selected from the group consisting of amino, thiol, and hydroxyl moieties.

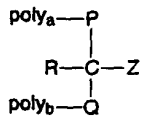
50. The method of Claim 44 wherein the active sites on the linker moiety are nucleophilic moieties selected from the group consisting of amino, thiol, and hydroxyl moieties.

51. The method of Claim 44 wherein the active sites on the linker moiety are electrophilic moieties selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde, vinylsulfone, maleimide, iodoacetamide, and iminoesters.

52. The method of Claim 51 wherein the active ester is N-hydroxylsuccinimidyl ester and the active carbonates are selected from the group consisting of N-hydroxylsuccinimidyl carbonate, *p*-nitrophenylcarbonate, and trichlorophenylcarbonate.

53. The method of Claim 44 wherein the hydrolytically stable linkages are selected from the group consisting of amide, amine, ether, carbamate, thiourea, urea, thiocarbamate, thiocarbonate, thioether, thioester, and dithiocarbamate linkages.

54. A method for preparing a polymeric derivative represented by the structure



comprising the steps of:

a) reacting nonpeptidic, water soluble, monofunctional polymers of the structure poly$_a$-W and poly$_b$-W with a linker moiety having at least two active sites for which W is selective, a reactive site Z for which W is not selective, and a moiety R which is substantially nonreactive, wherein W is an active electrophilic moiety selected from the group consisting of trifluoroethylsulfonate, isocyanate, isothiocyanate, active esters, active carbonates, aldehyde,

vinylsulfone, maleimide, iodoacetamide, and iminoesters, and may be the same or different on $poly_a$ and $poly_b$, wherein $poly_a$ and $poly_b$ are polymer moieties selected from the group consisting of poly(ethylene glycol), poly(vinyl alcohol), poly(propylene glycol), poly(oxyethylated glycerol), poly(oxyethylated sorbitol), poly(oxyethylated glucose), poly(oxazoline), poly(acryloylmorpholine), and poly(vinylpyrrolidone) and may be the same or different, and wherein the active sites of the linker moiety are nucleophilic sites selected from the group consisting of amino, thiol, and hydroxyl; and

b) forming hydrolytically stable linkages P and Q, which may be the same or different, in the absence of aromatic rings between the polymer and the linker moiety that are selected from the group consisting of amide, amine, ether, carbamate, thiourea, urea, thiocarbamate, thiocarbonate, thioether, thioester, and dithiocarbamate linkages.

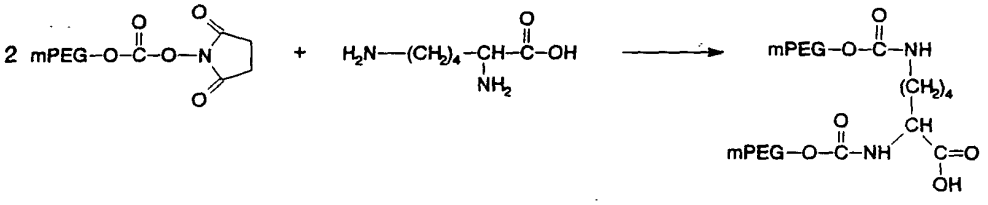
55. The method of Claim 54 wherein the linker moiety is substituted with polymer at each active site in one step.

56. The method of Claim 55 wherein the linker moiety is substituted with polymer at each active site in more than one step.

57. The multi-armed polymeric derivative of Claim 54 wherein said linker moiety is selected from the group consisting of monohydroxy alcohols and monocarboxilic acids having two or more active moieties selected from the group consisting of thiol, amino, and hydroxyl moieties.

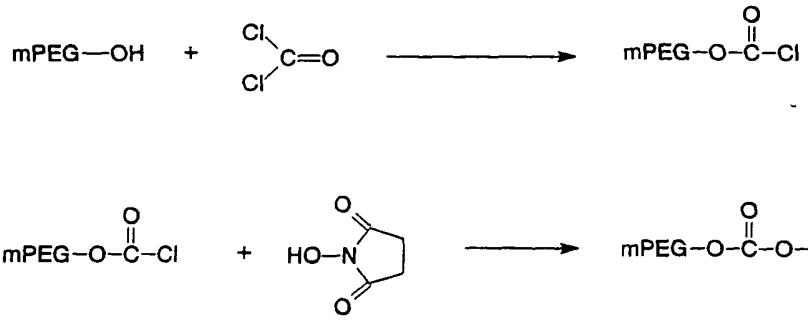
58. The multi-armed polymeric derivative of Claim 1 wherein Z is selected from the group consisting of carboxyl, hydroxyl, activated carboxyl, activated hydroxyl, and conjugates of precursor activated carboxyl or hydroxyl sites and molecules having sites for which said precursor activated sites are active.

59. A method for forming monofunctional monomethoxy-poly(ethylene glycol) disubstituted lysene comprising the following step:



60. The method of Claim 59 wherein the reaction takes place in water at a pH of about 8.0.

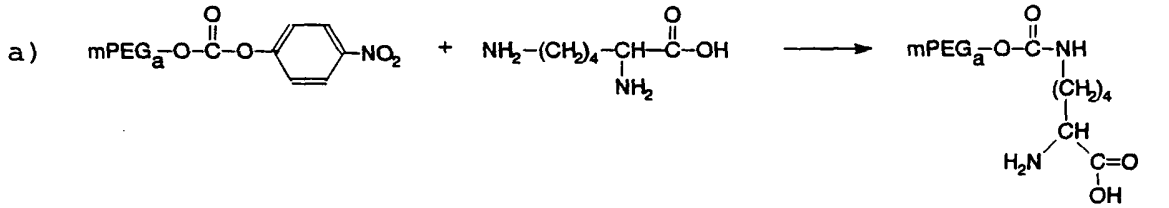
61. The method of Claim 59 further comprising the steps of

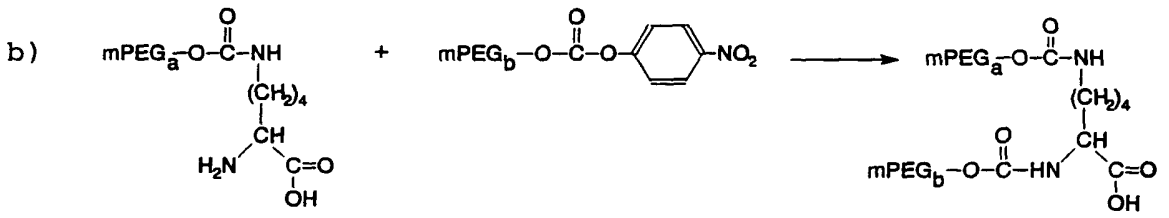


62. The method of Claim 61 wherein steps a) and b) take place in methylene chloride.

63. The method of Claim 59 further comprising the steps of activating the carboxyl moiety and reacting the activated carboxyl moiety with an active moiety to join the disubstituted lysine to the active moiety.

64. A method for forming a monofunctional monomethoxy-poly(ethylene glycol) disubstituted compound comprising the following steps:





65. The method of Claim 64 further comprising the steps of activating the carboxyl moiety and reacting the activated carboxyl moiety with an active moiety to join the disubstituted lysine to the active moiety.

66. The method of Claim 64 wherein step a) takes place in aqueous buffer.

67. The method of Claim 64 wherein step b) takes place in methylene chloride.